



GAGCTCGGAT	CCACTACTCG	ACCCACGCGT	CCGGCCAGGA	CCTCTGTGAA	CCGGTCGGGG	60
CGGGGGCCGC	CTGGCCGGGA	GTCTGCTCGG	CGGTGGGTGG	CCGAGGAAGG	GAGAGAACGA	120
TCGCGGAGCA	GGGCGCCCGA	ACTCCGGGCG	CCGCGCC	ATG CGC CGG	GCC AGC CGA	175
		Met Arg	Arg Ala	Ser Arg		
		1		5		
GAC TAC GGC	AAG TAC CTG	CGC AGC TCG	GAG GAG ATG	GGC AGC GGC	CCC	223
Asp Tyr Gly	Lys Tyr Leu	Arg Ser Ser	Glu Met Gly	Ser Gly Pro		
	10	15	20			
GGC GTC CCA	CAC GAG GGT	CCG CTG CAC	CCC GCG CCT	TCT GCA CCG	GCT	271
Gly Val Pro	His Glu Gly	Pro Leu His	Pro Ala Pro	Ser Ala Pro	Ala	
	25	30	35			
CCG GCG CCG	CCA CCC GCC	TCC CGC TCC	ATG TTC CTG	GCC CTC CTG		319
Pro Ala Pro	Pro Pro Ala	Ser Arg Ser	Met Phe Leu	Ala Leu Leu		
	40	45	50			

FIG.1A

GGG CTG GGA CTG GGC CAG GTG GTC TGC AGC ATC GCT CTG TTC CTG TAC	367
Gly Leu Gly Leu Gly Gln Val Val Cys Ser Ile Ala Leu Phe Leu Tyr	
55 60 65 70	
TTT CGA GCG CAG ATG GAT CCT AAC AGA ATA TCA GAA GAC AGC ACT CAC	415
Phe Arg Ala Gln Met Asp Pro Asn Arg Ile Ser Glu Asp Ser Thr His	
75 80 85	
TGC TTT TAT AGA ATC CTG AGA CTC CAT GAA AAC GCA GGT TTG CAG GAC	463
Cys Phe Tyr Arg Ile Leu Arg Leu His Glu Asn Ala Gly Leu Gln Asp	
90 95 100	
TCG ACT CTG GAG AGT GAA GAC ACA CTA CCT GAC TCC TGC AGG AGG ATG	511
Ser Thr Leu Glu Ser Glu Asp Thr Leu Pro Asp Ser Cys Arg Arg Met	
105 110 115	
AAA CAA GCC TTT CAG GCG GCC GTG CAG AAG GAA CTG CAA CAC ATT GTG	559
Lys Gln Ala Phe Gln Gly Ala Val Gln Lys Glu Leu Gln His Ile Val	
120 125 130	

FIG.1B

GGG CCA CAG CGC TTC TCA GGA GCT CCA GCT ATG ATG GAA GGC TCA TGG	607
Gly Pro Gln Arg Phe Ser Gly Ala Pro Ala Met Met Glu Gly Ser Trp	
135 140 145 150	
TTG GAT GTG GCC CAG CGA GGC AAG CCT GAG GCC CAG CCA TTT GCA CAC	655
Leu Asp Val Ala Gln Arg Gly Lys Pro Glu Ala Gln Pro Phe Ala His	
155 160 165	
CTC ACC ATC AAT GCT GCC AGC ATC CCA TCG GGT TCC CAT AAA GTC ACT	703
Leu Thr Ile Asn Ala Ala Ser Ile Pro Ser Gly Ser His Lys Val Thr	
170 175 180	
CTG TCC TCT TGG TAC CAC GAT CGA GGC TGG GCC AAG ATC TCT AAC ATG	751
Leu Ser Ser Trp Tyr His Asp Arg Gly Trp Ala Lys Ile Ser Asn Met	
185 190 195	

FIG.1C

ACG TTA AGC AAC GGA AAA CTA AGG GTT AAC CAA GAT GGC TTC TAT TAC	799
Thr Leu Ser Asn Gly Lys Leu Arg Val Asn Gln Asp Gly Phe Tyr Tyr	
200 205 210	
CTG TAC GCC AAC ATT TGC TTT CGG CAT CAT GAA ACA TCG GGA AGC GTA	847
Leu Tyr Ala Asn Ile Cys Phe Arg His His Glu Thr Ser Gly Ser Val	
215 220 225 230	
CCT ACA GAC TAT CTT CAG CTG ATG GTG TAT GTC GTT AAA ACC AGC ATC	895
Pro Thr Asp Tyr Leu Gln Leu Met Val Tyr Val Val Lys Thr Ser Ile	
235 240 245	
AAA ATC CCA AGT TCT CAT AAC CTG ATG AAA GGA GGG AGC ACG AAA AAC	943
Lys Ile Pro Ser Ser His Asn Leu Met Lys Gly Gly Ser Thr Lys <u>Asn</u>	
250 255 260	
TGG TCG GGC AAT TCT GAA TTC CAC TTT TAT TCC ATA AAT GTT GGG GGA	991
Trp Ser Gly Asn Ser Glu Phe His Phe Tyr Ser Ile Asn Val Gly Gly	
265 270 275	

FIG.1D

TTT	TTC	AAG	CTC	CGA	GCT	GGT	GAA	GAA	ATT	AGC	ATT	CAG	GTG	TCC	AAC	1039
Phe	Phe	Lys	Leu	Arg	Ala	Gly	Glu	Glu	Ile	Ser	Ile	Gln	Val	Ser	<u>Asn</u>	
	280					285			290							
CCT	TCC	CTG	CTG	GAT	CCG	GAT	CAA	GAT	GCG	ACG	TAC	TTT	GGG	GCT	TTC	1087
Pro	Ser	Leu	Leu	Asp	Pro	Asp	Gln	Asp	Ala	Thr	Tyr	Phe	Gly	Ala	Phe	
295					300					305					310	
AAA	GTT	CAG	GAC	ATA	GAC	T	GAGACTCATT	TCGTGGAACA	TTAGCATGGA							1136
Lys	Val	Gln	Asp	Ile	Asp											
						315										
TGTCCTAGAT	GTTTGGAAC	TTCTTAAAA	ATGGATGATG	TCTATACATG	TGTAAGACTA											1196
CTAAGAGACA	TGGCCCACGG	TGTATGAAAC	TCACAGCCCCT	CTCTCTTGAG	CCTGTACAGG											1256
TTGTGTATAT	GTAAGTCCA	TAGGTGATGT	TAGATTTCATG	GTGATTACAC	AACGGTTTAA											1316

FIG.1E

CAATTTTGTA ATGATTTCCCT AGAATTGAAC CAGATTGGGA GAGTATTCC GATGCTTATG	1376
AAAAACTTAC ACGTGAGCTA TGGAAAGGGG TCACAGTCTC TGGGTCTAAC CCCTGGACAT	1436
GTGCCACTGA GAACCTTGAA ATTAAGAGGA TGCCATGTCA TTGCAAAGAA ATGATAGTGT	1496
GAAGGGTTAA GTTCTTTTGA ATTGTTACAT TGCGCTGGGA CCTGCAAATA AGTTCTTTT	1556
TTCTAATGAG GAGAGAAAAA TATATGTATT TTTATATAAT GTCTAAAGTT ATATTTCAGG	1616
TGTAATGTTT TCTGTGCAAA GTTTTGTAAA TTATATTTGT GCTATAGTAT TTGATTCAAA	1676
ATATTTAAA ATGTCTCACT GTTGACATAT TTAATGTTTT AAATGTACAG ATGTATTTAA	1736
CTGGTGCAC TTGTAATTCC CCTGAAGGTA CTCGTAGCTA AGGGGCAGA ATACTGTTC	1796
TGGTGACCAC ATGTAGTTTA TTTCTTTATT CTTTTAACT TAATAGAGTC TTCAGACTTG	1856

FIG.1F

TCAAAACTAT GCAAGCAAAA TAAATAAATA AAAATAAAAT GAATACCTTG AATAATAAGT	1916
AGGATGTTGG TCACCAGGTG CCTTTCAAAT TTAGAAGCTA ATTGACTTTA GGAGCTGACA	1976
TAGCCAAAAA GGATACATAA TAGGCTACTG AAATCTGTCA GGAGTATTTA TGCAATTATT	2036
GAACAGGTGT CTTTTTTTAC AAGAGCTACA AATTGTAAAT TTTGTTTCTT TTTTTTCCCA	2096
TAGAAAATGT ACTATAGTTT ATCAGCCAAA AAACAATCCA CTTTTTAATT TAGTGAAAAGT	2156
TATTTTATTA TACTGTACAA TAAAAGCATT GTCTCTGAAT GTTAATTTTT TGGTACAAAA	2216
AATAAATTG TACGAAAACC TGAAAAAAA AAAAAAAA AAAAAGGG CGGCCGCTCT	2276
AGAGGGCCCT ATTCTATAG	2295

FIG.1G

FIG. 2A

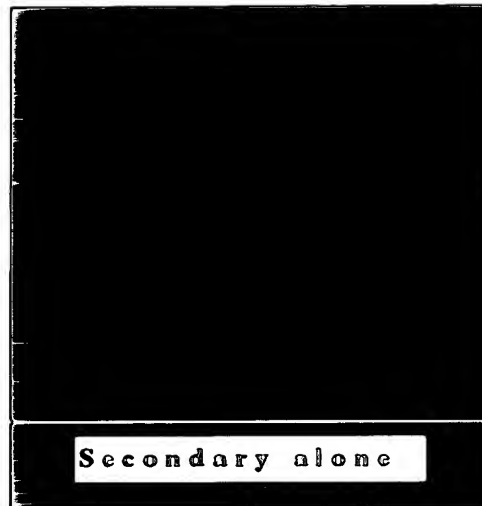


FIG. 2B

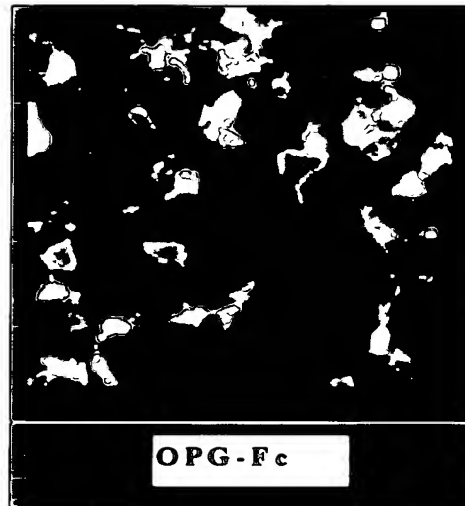
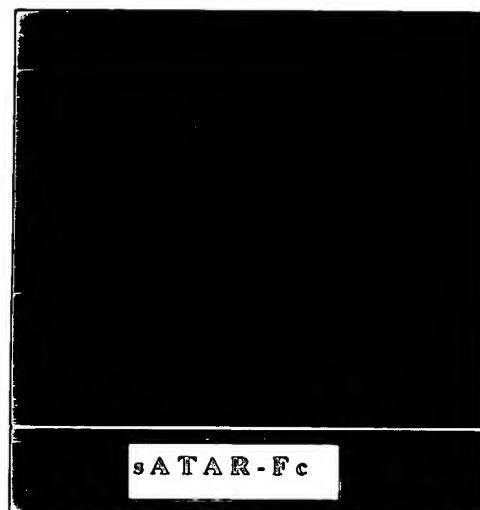


FIG. 2C



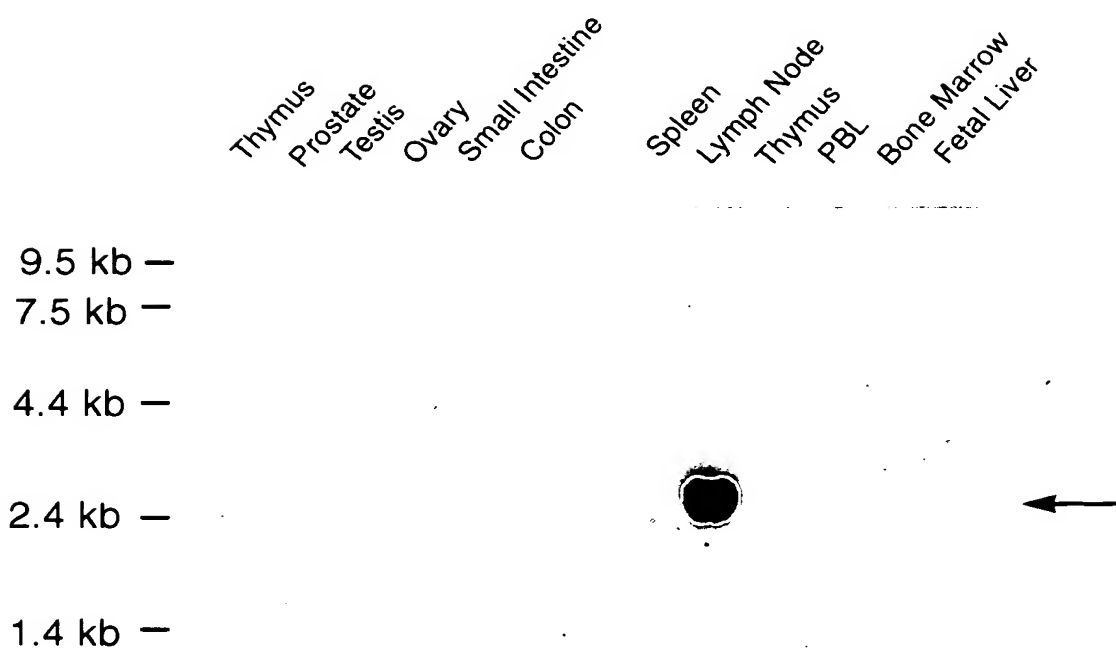


FIG.3

10 30 50
AAGCTTGGTACCGAGCTCGGATCCACTACTCGACCCACGCTCCGGCGCCCGAGGCC

70 90 110
AAAGCCGGGCTCCAAGTCGGCGGCCACGTGAGGCTCCGCCGAGCCTCCGGAGTTGGC

130 150 170
CGCAGACAAGAAGGGAGGAGCGGGAGAGGGAGAGAGCTCCGAAGCAGAGGCCGAG

190 210 230
CGCCATGCGCGCGCCAGCAGAGACTACACCAAGTACCTGCGTGGCTCGGAGAGATGGG
M R R A S R D Y T K Y L R G S E M G

250 270 290
CGGCGGCCCCGAGCCCCGACGAGGGCCCCCTGCACGCCCGCCGCTCGCCGCA
G G P G A P H E G P L H A P P P A P H

310 330 350
CCAGCCCCCGCGCTCCCGCTCCATGTTCTGTCGGCCCTCCTGGGGCTGGGGTGGCCA
Q P P A A S R S M F V A L L G L G L G Q

370 390 410
GGTGTCTGCAGCGTCGCCCTGTCTTCTTATTTTCAGAGCGCAGATGGATCCTAATAGAAT
V V C S V A L F F Y F R A Q M D P N R I

FIG.4A

430 450 470
ATCAGAAGATGGCACTCACTGCATTTATAGAATTTTGAGACTCCATGAATGCAGATTT
S E D G T H C I Y R I L R L H E N A D F

490 510 530
TCAAGACACAACCTCTGGAGAGTCAAGATACAAATTAATACCTGATTCATGTAGGAGAAT
Q D T T L E S Q D T K L I P D S C R R I

550 570 590
TAAACAGGCCTTTCAAGGAGCTGTGCAAAAGGAATTACAACATATCGTTGGATCACAGCA
K Q A F Q G A V Q K E L Q H I V G S Q H

610 630 650
CATCAGAGCAGAGAAAGCGATGGTGGATGGCTCATGGTTAGATCTGGCCAAAGAGGAGCAA
I R A E K A M V D G S W L D L A K R S K

670 690 710
GCTTGAAGCTCAGCCTTTTGCTCATCTCACTATTAATGCCACCGACATCCCATCTGGTTC
L E A Q P F A H L T I N A T D I P S G S

730 750 770
CCATAAAGTGAGTCTGTCCTCTTGGTACCATGATCGGGGTGGGCCAAGATCTCCAACAT
H K V S L S S W Y H D R G W A K I S N M

FIG.4B

```

790                               810                               830
GACTTTAGCAATGGAAACTAATAGTTAATCAGGATGGCTTTTATTACCTGTATGCCAA
T F S N G K L I V N Q D G F Y Y L Y A N

850                               870                               890
CATTTGCTTTCGACATCATGAACCTTCAGGAGACCTAGCTACAGAGTATCTTCAACTAAT
I C F R H H E T S G D L A T E Y L Q L M

910                               930                               950
GGTGACGTCACTAAACCAGCATCAAAATCCCAAGTTCTCATACCTGATGAAAGGAGG
V Y V T K T S I K I P S S H T L M K G G

970                               990                               1010
AAGCACCAAGTATTGGTCAGGGAATTCTGAATTCCCATTTTATTCCATAAACGTTGTGG
S T K Y W S G N S E F H F Y S I N V G G

1030                             1050                             1070
ATTTTTTAAGTTACGGTCTGGAGAGGAAATCAGCATCGAGGTCTCCAAACCCCTCTTACT
F F K L R S G E E I S I E V S N P S L L

1090                             1110                             1130
GGATCCGGATCAGGATGCAACATACTTTGGGGCTTTTAAAGTTCGAGATATAGATTGAGC
D P D Q D A T Y F G A F K V R D I D

```

FIG.4C

```
1150          1170          1190
CCGAGTTTGGAGGTGTTATGTATTTCCCTGGATGTTTGGAAACATTTTTTAAACAAGCC

1210          1230          1250
AAGAAAGATGTATATAGGTGTGTGAGACTACTAAGAGGCATGGCCCCAACGGTACACGAC

1270          1290          1310
TCAGTATCCATGCTCTTGACCTTGTAGAGAAACACCGCGTATTTACAGCCAGTGGGAGATGT

1330          1350          1370
TAGACTCATGGTGTGTACACAATGGTTTTTTAAATTTTGTAATGAATTCCTAGAAATTAA

1390          1410          1430
CCAGATTGGAGCAATTACGGGTGACCTTATGAGAAACTGCATGTGGGCTATGGGAGGGG
```

FIG.4D

1450 1470 1490
TTGGTCCCCTGGTCATGTGCCCCCTTCGCAGCTGAAGTGGAGAGGGTGTCTCATCTAGCGCAAT

1510 1530 1550
TGAAGGATCATCTGAAGGGGCAAATTCTTTTGAAATTGTTACATCATGTGGAACCTGCAA

1570 1590 1610
AAAATACTTTTCTAAATGAGGAGAGAAATATATGTATTTTATATAATACTAAAGTTA

1630 1650 1670
TATTTACAGATGTAATGTTTTCTTTGCAAGTATTGTAAATTATATTTGTGCTATAGTATT

1690 1710 1730
TGATTCAAATAATTTAAATGCTCTTGCTGTGACATATTTAATGTTTAAATGTACAGA

1750 1770 1790
CATATTTAAGTGTGCACCTTTGTAAATTCCCTGGGAAACTGCAGCTAAGGAGGGGAA

1810 1830 1850
AAAAATGTTGTTCCCTAATATCAAATGCAGTATATTTCTTCGTTCTTTTAAAGTTAATAG

FIG.4E

1870	1890	1910
ATTTTTTCAGACTTGTCAAGCCTGTGCAAAAATTA		AAATGGATGCCCTTGAATAATAAG
1930	1950	1970
CAGGATGTTGGCCACCAGGTGCCCTTTCAAAATTTAGAACTAATTGACTTTAGAAAGCTGA		
1990	2010	2030
CATTGCCAAAAGGATACATAATGGGCCCACTGAAATCTGTCAAGAGTAGTTATATAATTG		
2050	2070	2090
TTGAACAGGTGTTTTTCCACAAGTGCCGCAAAATTGTACCTTTTTTTTTTTTCAAAATAG		
2110	2130	2150
AAAAGTTATTAGTGTTTATCAGCAAAAAGTCCAATTTTAATTAGTAAATGTTATCTT		
2170	2190	2210
ATACTGTACAATAAAAACATTGCCCTTTGAAATGTTAATTTTTTGGTACAAAAATAATTTA		
2230	2250	2270
TATGAAAAAAAAGGGCGCGCTCTAGAGGGCCCTATTCTATAG		

FIG.4F

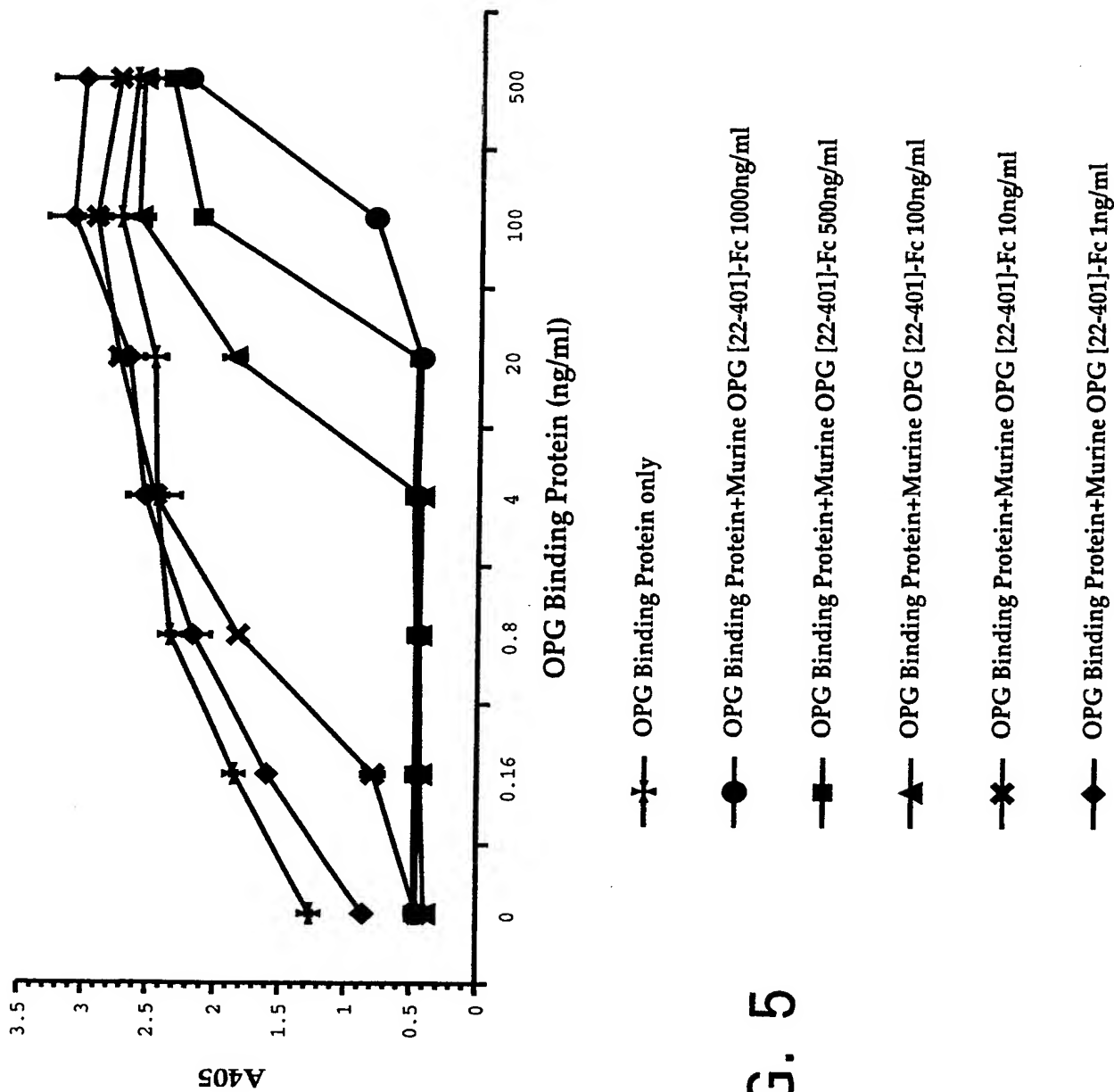


FIG. 5

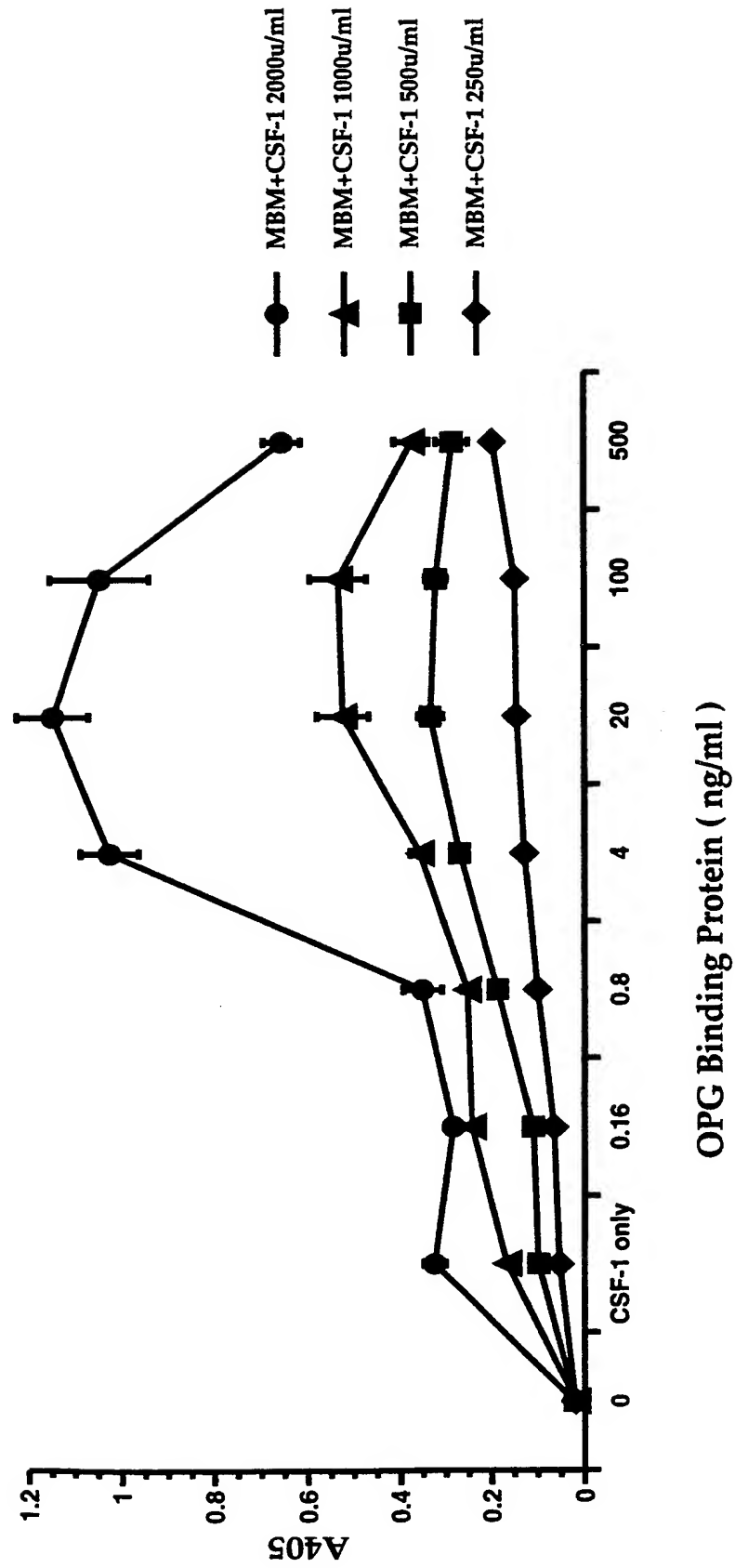
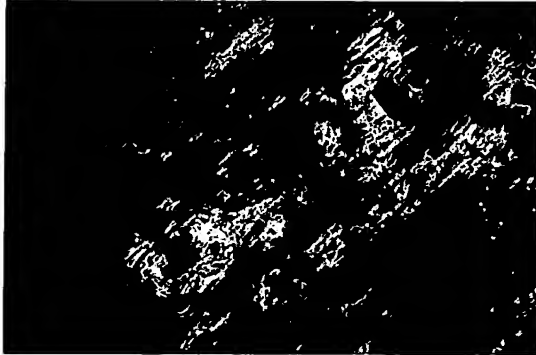


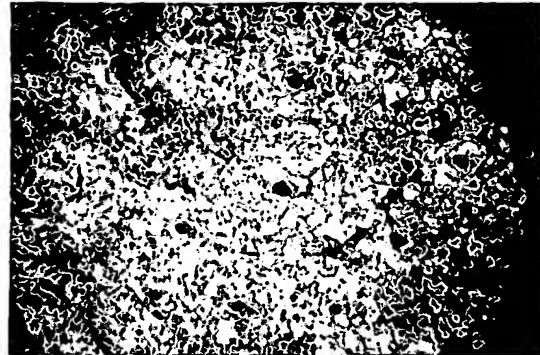
FIG. 6

FIG.7A

Toluidine Blue Staining



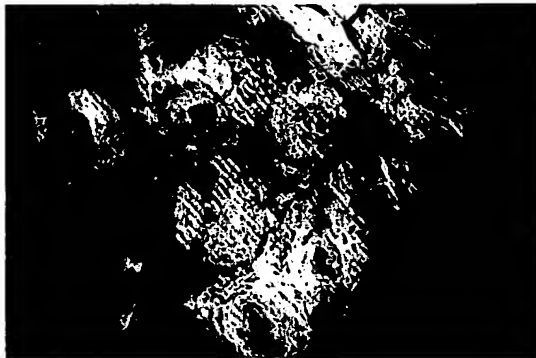
TRAP staining



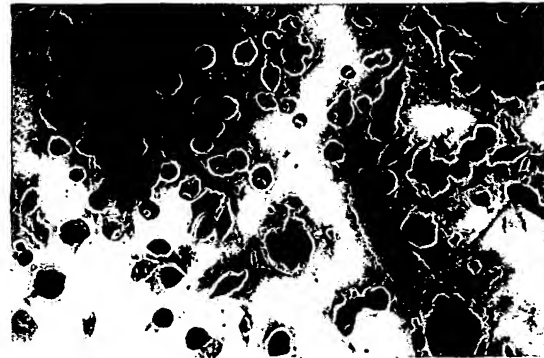
Bone Marrow Cells + M-CSF-1

FIG.7B

Toluidine Blue Staining



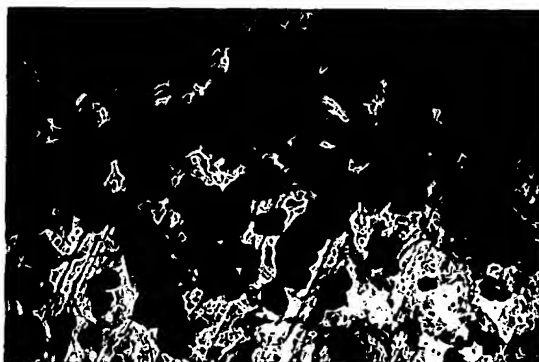
TRAP staining



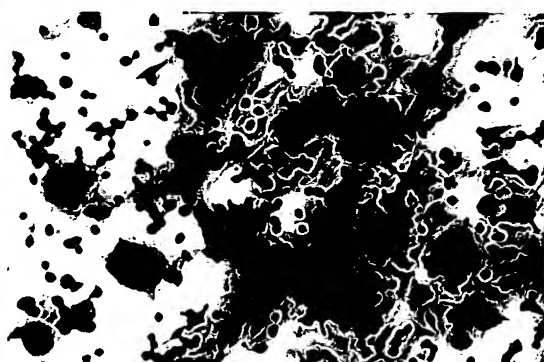
Bone Marrow Cells + OPG Binding Protein

FIG.7C

Toluidine Blue Staining



TRAP staining



Bone Marrow Cells + M-CSF-1 + OPG Binding Protein

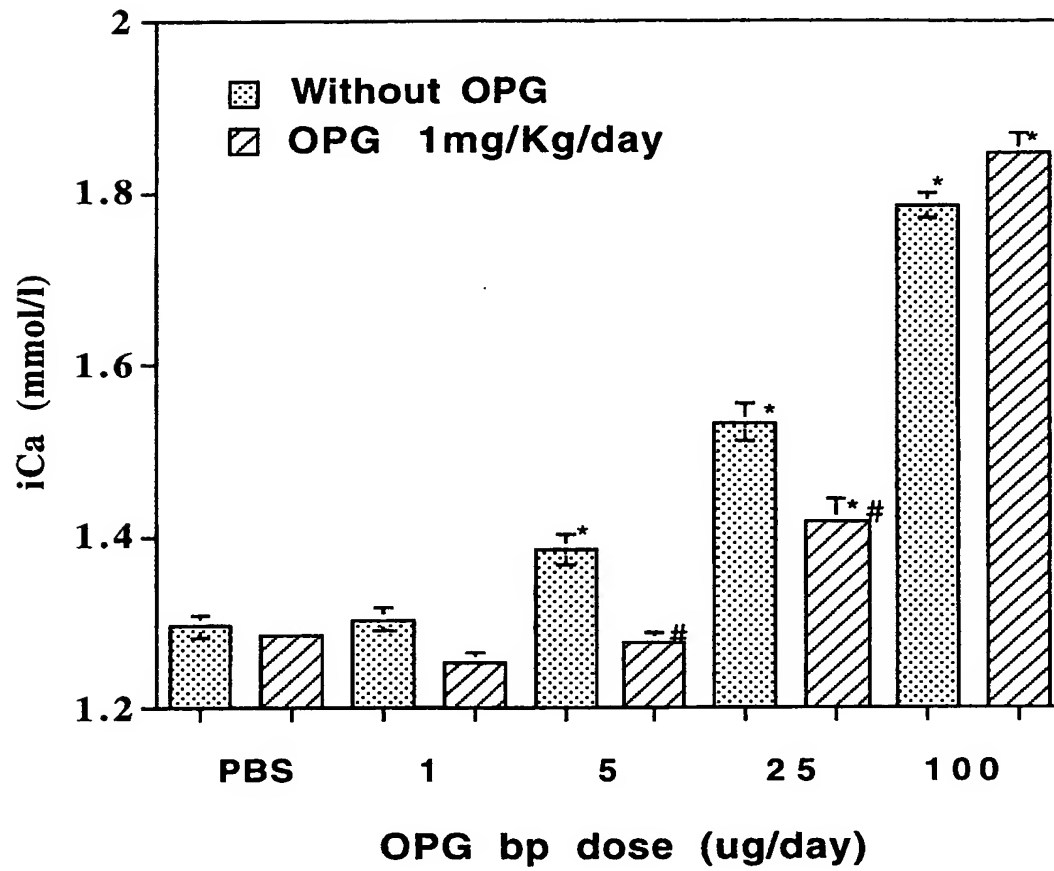


FIG. 8

PBS



FIG.9A

OPGbp 5ug/d



FIG.9B

OPGbp 25ug/d



FIG.9C

OPGbp100ug/d



FIG.9D

10	30	50
ACTCGACCCACGGCTCCGCCGCCGCCGACCGCGCCATGGACCCGCGCGCGCGCGGCC		
		<u>M D P R A R R R</u>
70	90	110
GCCAGCTGCCCGCGCGCTGCTGGCGCTCTGCGTGTGCTGCTCCACTGCAGGTGACTC		
<u>Q L P A P L L A L C V L L V P L Q V T L</u>		
130	150	170
TCCAGTCACTCCTCCATGCACCCAGGAGAGGCATTATGAGCATCTCGGACGGTGTGCA		
Q V T P P C T Q E R H Y E H L G R C C S		
190	210	230
GCAGATGCCGAACCAGGAAAGTACCTGTCTCTTAAGTGCACTCCTACCTCCGACAGTGTGT		
R C E P G K Y L S S K C T P T S D S V C		
250	270	290
GTCTGCCCTGTGGCCCCGATGAGTACTTGGACACCTGGAATGAAGAAGATAAATGCTTGC		
L P C G P D E Y L D T W N E E D K C L L		
310	330	350
TGCATAAAGTCTGTGATGCAGGCAAGGCCCTGGTGGCGGTGGATCCTGGCAACCAACCGG		
H K V C D A G K A L V A V D P G N H T A		

FIG.10A

370 390 410
CCCCGGCTCGCTGCTGCTTGCACGGCTGGCTACCACTGGAACCTCAGACTGCGAGTGTGCTGCC
P R R C A C T A G Y H W N S D C E C C R
430 450 470
GCAGGAACACGGAGTGTGCACCTGGCTTCGGAGCTCAGCATCCCCTTGCAGCTCAACAAGG
R N T E C A P G F G A Q H P L Q L N K D
490 510 530
ATACGGTGTGCACACCCCTGCCCTCCTGGGCTTCTCTCAGATGTCTTTTCGTCCACAGACA
T V C T P C L L G F F S D V F S S T D K
550 570 590
AATGCAAAACCTTGGACCAACTGCACCCCTCCCTTGGAAAGCTAGAAGCACACCGGGACAA
C K P W T N C T L L G K L E A H Q G T T
610 630 650
CGGAATCAGATGGTCTGCAGCTCTTCCATGACACTGAGGAGACCCCAAGGAGGCC
E S D V V C S S S M T L R R P P K E A Q

FIG.10B

670 690 710
 AGGCTTACCTGCCAGTCTCATCGTTCTGCTCCTCTTTCATCTCTGTGGTAGTAGTGGCTG
 A Y L P S L I V L L L L F I S V V V V A A
 730 750 770
 CCATCATCTTCGGCGTTTACTACAGGAAGGAGGAAAGCGCTGACAGCTAATTTGTGGA
 I I F G V Y Y R K G G K A L T A N L W N
 790 810 830
 ATTGGTCAATGATGCTTGCAGTAGTCTAAGTGGAATAAGGAGTCCCTCAGGGACCGTT
 W V N D A C S S L S G N K E S S G D R C
 850 870 890
 GTGCTGGTTCCCACTCGGCAACCTCCAGTCAGCAAGAAGTGTGTAAGGTATCTTACTAA
 A G S H S A T S S Q Q E V C E G I L L M
 910 930 950
 TGACTCGGAGGAGAAGATGGTTCCAGAACGACGGTGCTGGAGTCTGTGGGCCCTGTGTGTG
 T R E E K M V P E D G A G V C G P V C A
 970 990 1010
 CGGCAGGTGGGCCCTGGCAGAAAGTCAGAGATTCTAGGACGTTTCACACTGGTCAGCGAGG
 A G G P W A E V R D S R T F T L V S E V

FIG.10C

1030	1050	1070
TTGAGACGCAAGGAGACCTCTCGAGGAAGATTCCACAGAGGATGAGTACACGACCGGC		
E T Q G D L S R K I P T E D E Y T D R P		
1090	1110	1130
CCTCGCAGCCTTCGACTGGTTCACCTGCTCCTAATCCAGCAGGGAAGCAATCTATACCCC		
S Q P S T G S L L L I Q Q G S K S I P P		
1150	1170	1190
CATTCCAGGAGCCCTGGAAGTGGGGAGAACGACAGTTTAAGCCAGTGTTCACCCGGA		
F Q E P L E V G E N D S L S Q C F T G T		
1210	1230	1250
CTGAAAGCACGGTGGATTCTGAGGGCTGTGACTTCACCTGAGCCTCCGAGCAGAACTGACT		
E S T V D S E G C D F T E P P S R T D S		
1270	1290	1310
CTATGCCCGTGTCCTGAAAGCACCTGACAAAGAAATAGAAAGTGACAGTTGCCCTCC		
M P V S P E K H L T K E I E G D S C L P		
1330	1350	1370
CCTGGGTGCTCCTCAACTCAACAGATGGCTACACAGGCAGTGGAACACTCCTGGGG		
W V V S S N S T D G Y T G S G N T P G E		

FIG.10D

1390 1410 1430
AGGACCATGAACCCCTTTCCAGGGTCCCTGAAATGTGACCATTGCCCCAGTGTGCCTACA
D H E P F P G S L K C G P L P Q C A Y S
1450 1470 1490
GCATGGGCTTTCCACAGTGAAGCAGCAGCCAGCATGGCAGAGCGGGAGTACGGCCCCCAGG
M G F P S E A A A S M A E A G V R P Q D
1510 1530 1550
ACAGGGCTGATGAGAGGGAGCCCTCAGGGTCCGGAGCTCCCCCAGTGACCCACCTG
R A D E R G A S G S G S P S D Q P P A
1570 1590 1610
CCTCTGGGAACGTGACTGGAACAGTAACTCCACGTTCATCTAGCGGGCAGGTGATGA
S G N V T G N S N S T F I S S G Q V M N
1630 1650 1670
ACTTCAAGGTGACATCATCGTGGTGTATGTACGCCAGACCCTCGCAGGAGGGCCCGGTT
F K G D I I V V Y V S Q T S Q E G P G S
1690 1710 1730
CCGCAGAGCCCGAGTCGGAGCCCGTGGGGCCCGCTGTGCAGGAGGACGCTGGCACACA
A E P E S E P V G R P V Q E E T L A H R

FIG.10E

1750 1770 1790
 GAGACTCCTTTGCGGGCACCGCGCCGGCTTCCCGACGTCGTGCCACCGGGCTGGGC
 D S F A G T A P R F P D V C A T G A G L
 1810 1830 1850
 TGCAGGAGAGGGGACCCCGGCAGAGGACGGACATCCGGCCGGTGCAGGAGCAGG
 Q E Q G A P R Q K D G T S R P V Q E Q G
 1870 1890 1910
 GTGGGCGCAGACTTCACTCCATACCCAGGGGTCCGGACAATGTGCAGAATGACCTCACC
 G A Q T S L H T Q G S G Q C A E
 1930 1950 1970
 TTCTCTGTCTGCCCTGGGTGCAGGGCACCCAGTGCCCTTTCCAAAACATGGTGTAGCTAGC
 1990 2010 2030
 CACTGTGCACCTCCTCACTGGTGCAGGCTGCTGGCATGGTGATGGAGCCCACCTCTCACT
 2050 2070
 TCCTCCAGTGCCCCCTCTCCTCTGCCCTCCTAC

FIG.10F

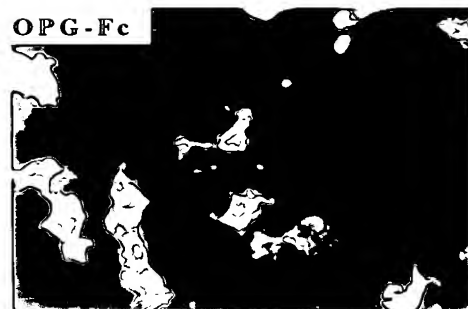
FIG. 11A



FIG. 11B



FIG. 11C



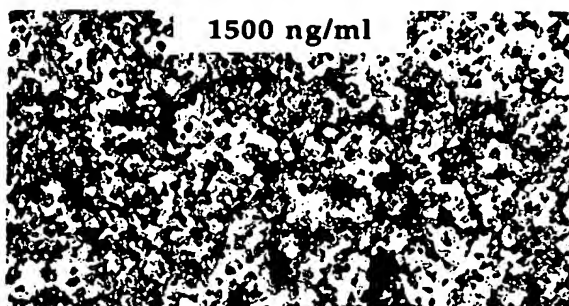


FIG.12A

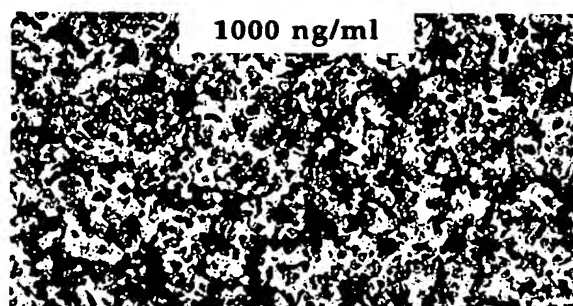


FIG.12B

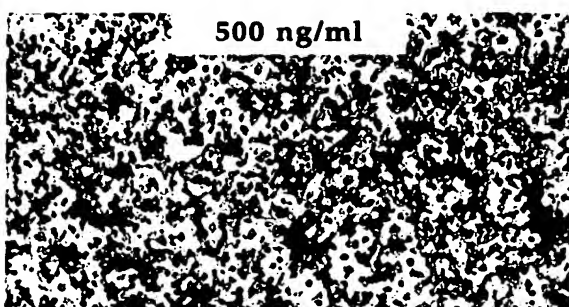


FIG.12C

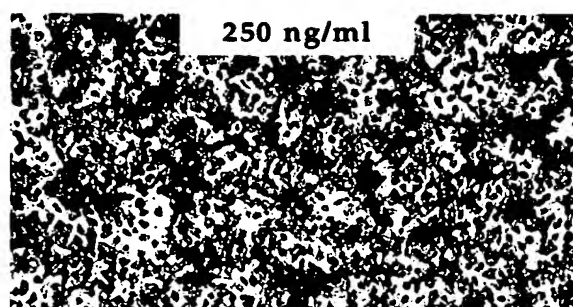


FIG.12D

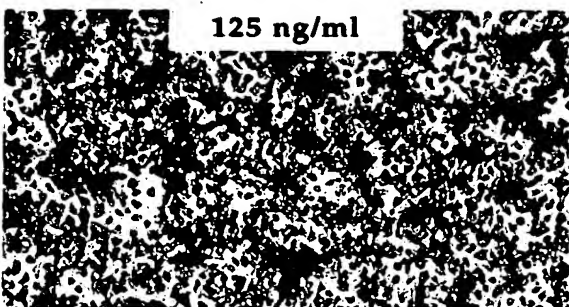


FIG.12E

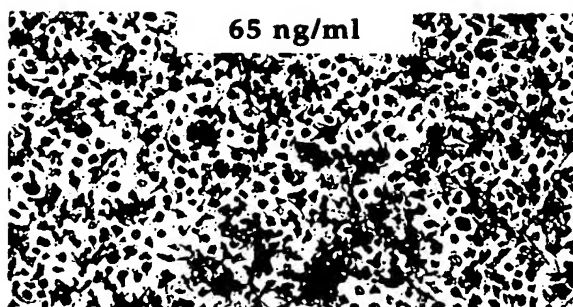


FIG.12F

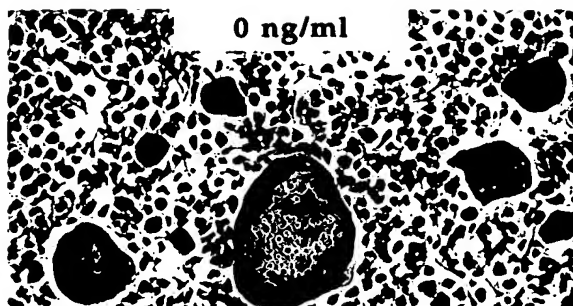
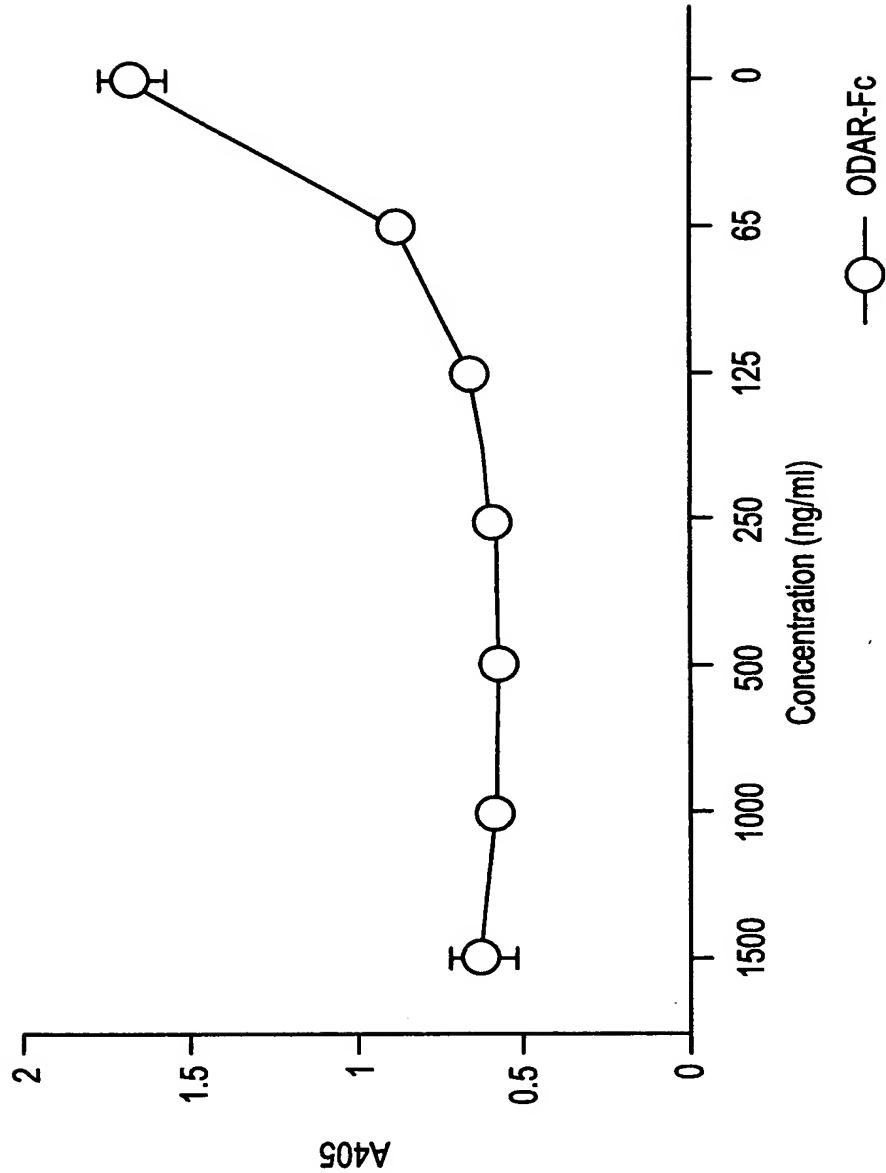
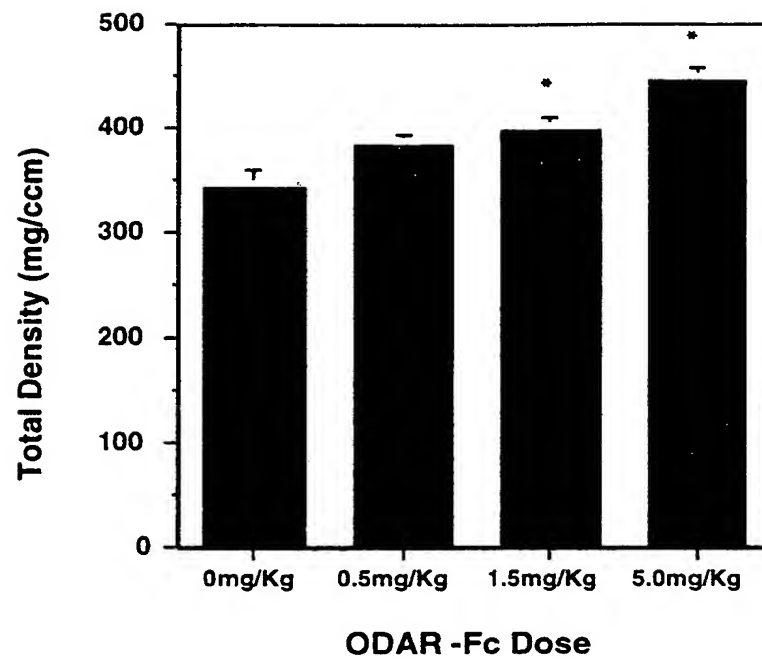


FIG.12G

FIG. 12H





* Different to vehicle treated control $p < 0.05$.

FIG.13